

'A Versatile Remedy'

'Benzedrine' Tablets

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'BENZEDRINE'— $C_6H_5.CH_2.CH(NH_2)CH_3$ —is a sympathomimetic compound that is structurally related to ephedrine and adrenaline. The sulphate of this compound—issued as 'Benzedrine' Tablets—has been found of value in a number of commonly-encountered clinical conditions, apparently dissimilar on the surface, but each requiring stimulation of the sympathetic and central nervous system as an essential therapeutic factor. It is, indeed, as the *Lancet* (1947, 1, 567) says, 'a versatile remedy.'

Wide Margin of Safety

Four conclusions concerning the general relative safety of 'Benzedrine' can fairly be drawn from the published literature: (1) The risk of undesirable reactions is negligible; (2) The chronic toxicity is low; (3) The acute toxicity is low; (4) The danger of habit-formation is minimal. The following quotations bear out these points:—

1. 'Occasional reactions may occur, including headache, restlessness, insomnia, irritability, palpitation, and a disturbance of the bowel habit. These are exceedingly rare and are merely mentioned to call attention to their rarity.' (PELNER, L. : *N.Y. St. J. Med.*, 1944, 44, 2596.)
2. 'We must conclude, therefore, that there is no evidence of physiological damage from Benzedrine even in prolonged and massive dosage.' (SHORVON, H. J. : *Brit. med. J.*, 1945, 2, 285.)
3. 'Addiction is relatively rare; if tolerance is being established, leaving off the drug for a few days will usually re-establish normal responsiveness. There are no withdrawal symptoms. Some constitutionally lethargic people demand it, and if they are benefited by it may be allowed to remain on it permanently; it is probable that in such persons it has a real part to play in remedying a constitutional inadequacy of the autonomic system or of bodily metabolism.' (SARGANT, W., and SLATER, E. (1948) : *An Introduction to Physical Methods of Treatment in Psychiatry*, p. 117.)
4. 'Most patients, such as narcoleptics and psychopaths, who take it ['Benzedrine'] continuously for years, display neither toxic signs nor increased tolerance. They can, moreover, discontinue the drug abruptly without craving or other withdrawal symptoms.' (*Lancet*, 1947, 1, 567.)

'Benzedrine' is the registered Trade Mark of Smith Kline & French International Co. to designate its brand of amphetamine.

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Depressive States

Over ten years ago Guttman and Sargant (1937) stated 'Mild depression accompanied by retardation is the most favourable of all psychological disorders for benzedrine therapy.' The truth of this statement has been substantiated by numerous writers ever since.

'Benzedrine' Tablets may be of great value in transforming the patient's gloomy outlook and restoring his capacity for physical and mental effort in the following types of depression : (1) Depression accompanying chronic organic disorders or persistent pain; (2) Depression characterized by chronic fatigue; (3) Depression due to grief over misfortune or bereavement; (4) Depression following acute infectious disease or surgical operations.

Watts (1947) noted that endogenous depression—'probably the most unpleasant illness anyone can contract'—is more common than is generally realized. He found 'Benzedrine' Tablets useful in dispelling early morning inertia and depression.

Houghton and Corrigan (1946), using amphetamine with patients undergoing institutional treatment for pulmonary tuberculosis, wrote :—

'The drug appears to have a definite value, particularly during difficult phases of thoracic surgery and for the restoration of confidence in the depressed or over-anxious patient. . . . In all cases . . . pains, headaches, and minor complaints disappeared. The beneficial effects observed . . . suggest that amphetamine might have a much wider application in general surgery.'

L. Fatti (1947) reported on a patient who was so depressed and exhausted after undergoing pneumonectomy that he had lost any hope of getting well. His spirits rose quickly on two 'Benzedrine' Tablets a day, and recovery was complete. The author was 'convinced that the raising of his spirits by amphetamine was the main factor in his survival'.

Dosage.—From 1 to 4 tablets (5-20 mg.) daily given in one or two doses before noon. If there is no response to 4 tablets daily, an increase is generally ineffective. After continued treatment with 'Benzedrine' some depressed patients seem to lose the beneficial effects which they

had previously experienced. In these cases the medication should be interrupted, and resumed after a suitable interval.

FATTI, L. (1947). *Lancet*, **1**, 344.

GUTTMANN, E., and SARGANT, W. (1937). *Brit. med. J.*, **1**, 1013.

HOUGHTON, L. E., and CORRIGAN, F. L. (1946). *Lancet*, **2**, 864.

WATTS, C. A. H. (1947). *Brit. med. J.*, **1**, 11.

Psychopathic States

According to Hill (1947), the most satisfactory psychopathic personalities to respond to amphetamine are 'those predominantly aggressive characters capable of warm interpersonal relationships, but continually wrecking such relationships . . . by impulsive irritability, minor acts of violence and intolerance of others'. The drug is described as bringing about a 'more integrated personality, a more mature expression of the primary appetitive drives'. Shorvon (1947) has made extensive use of the drug 'for adult psychopaths of the predominantly aggressive and predominantly inadequate types whose persistent abnormality of character generally showed itself in pathological emotionality, pathological or excessive sexuality, or asocial and amoral trends'.

Dosage.—Effective dosage varies with each case. An average useful dose is from 4 to 6 tablets a day, part being given in the morning and part at noon or early in the afternoon. Experience has shown that psychopaths tolerate even larger doses of the drug over long periods.

HILL, DENIS (1947). *Brit. J. Addict.*, **44**, 51.

SHORVON, H. J. (1947). *Ibid.*, **44**, 58.

Alcoholism

In a series of over 100 cases Reifenstein and Davidoff (1940) found that in the acute alcoholic psychoses the length of time necessary for recovery was considerably diminished by the use of 'Benzedrine'—frequently by half. In an earlier paper (1938) the same authors state that 'the headache, fatigue, languor, and mental retardation characteristic of a hang-over usually disappeared within an hour or so after a morning dose of from 5 to 10 mg.'

Bloomberg (1939) suggested that 'Benzedrine' permits a sufficient interval of sobriety for the institution of the more fundamental psychotherapeutic methods. 'There was no evidence whatsoever of addiction or habit formation to the drug.' Miller (1944) comments on the marked improvement in awareness, sensory perception, and activity drive obtained soon after treatment.

Dosage.—For *chronic alcoholism* 4 tablets daily, 2 on rising and 2 at noon. An increase or reduction may sometimes be necessary, and a third dose may be indicated if the patient expects to go out in the evening. For *alcoholic psychoses* 2 to 6 tablets daily, one half of the dose on rising and the other half at noon.

BLOOMBERG, W. (1939). *New Engl. J. Med.*, **220**, 129.

MILLER, M. M. (1944). *Amer. J. Psychiat.*, **100**, 800.

REIFENSTEIN, E. C., and DAVIDOFF, E. L. (1938). *J. Amer. med. Ass.*, **110**, 1811; (1940), *N.Y. St. J. Med.*, **40**, 247.

Behaviour Disorders of Children

The usefulness of 'Benzedrine' in behaviour disorders of children has been repeatedly pointed out since Bradley wrote in 1937 :—

'To see a single dose of benzedrine produce a greater improvement in school performance than the combined efforts of a capable staff working in a most favorable setting would have been all but demoralizing to the teachers, had not the improvement been so gratifying from a practical viewpoint.'

Recurrent bouts of aggressiveness and destructiveness may yield to 'Benzedrine' in what appears to be a specific way (Sargant and Slater, 1948). The noisy child becomes much more subdued; span of attention is lengthened in distractive children; interest in learning is stimulated; the activity of the hyperkinetic child becomes less disjointed; and co-operation, sociability, and behaviour are improved.

Children with nocturnal enuresis are usually deep sleepers. Braithwaite (1944) says, 'Rendering sleep less profound is best secured by benzedrine', and several clinicians agree on the drug's value in the sleepy, slow child. Molitch and Poliakoff (1937) report that in 12 of 14 boys who failed to respond to placebos the condition was completely relieved when they were given increasing doses of 'Benzedrine' up

to 5 tablets daily. They reverted to bedwetting within two weeks after they were taken off the drug.

Dosage.—Children appear to tolerate ‘Benzedrine’ remarkably well, but 1 to 4 tablets daily is usually recommended for behaviour disorders. In enuresis the drug should be given at bedtime ; start with small doses and increase until the optimum effect is obtained.

BRADLEY, C. (1937). *Amer. J. Psychiat.*, **94**, 577.

BRAITHWAITE, J. V. (1944). *Post-grad. med. J.*, **20**, 350.

MOLITCH, M., and POLIAKOFF, S. (1937). *Arch. Pediat.*, **54**, 499.

SARGANT, W., and SLATER, E. (1948). *Loc. cit.*, p. 116.

Narcolepsy

Treatment of narcolepsy was revolutionized in 1935 when Prinzmetal and Bloomberg advocated the use of ‘Benzedrine’ Tablets, which they found three times as effective as ephedrine in preventing attacks of sleep and in relieving cataplexy. According to Sargant and Slater (1948) ‘Benzedrine’ is now regarded as specific and diagnostic for narcolepsy.

Dosage.—Two tablets once daily to 8 tablets t.i.d. The requisite dosage, once attained, can be continued for years without increase.

PRINZMETAL, M., and BLOOMBERG, W. (1935). *J. Amer. med. Ass.*, **105**, 2051.

SARGANT, W., and SLATER, E. (1948). *Loc. cit.*, p. 114.

Post-encephalitic Parkinsonism

‘Benzedrine’ Tablets are a valuable adjunct to other forms of treatment in combating such symptoms as drowsiness, lethargy, depression, rigidity, tremor, and flat voice. The drug seems to act almost specifically in abolishing or reducing the number and severity of the oculogyric crises.

Dosage.—From 4 to 8 tablets daily, one-half of the dose at breakfast and the other half at noon. The best results have been obtained when the normal dosage of ‘Benzedrine’ was used in conjunction with the usual dose of stramonium, hyoscine, or atropine.

Brit. med. J., 1945, **1**, 245.

CRITCHLEY, M. (1941). *Practitioner*, **146**, 332.

HOFFMAN, H. L. (1941). *Brit. med. J.*, **1**, 816.

Overweight

‘Benzedrine’ is rationally indicated in the treatment of exogenous overweight because it : (1) Decreases appetite

and helps the patient to follow a diet ; (2) Increases activity and thus promotes a proper balance between energy output and caloric intake ; (3) Normally produces a sense of well-being and thus makes the patient less refractory to dietary restrictions ; (4) Often initiates new eating habits so that weight loss is maintained after withdrawal.

Ersner (1940) gave ' Benzedrine ' in doses of 1 to 6 tablets a day to over 500 obese patients, and studied 55 cases of ' pure overeating ' in detail. In spite of 5 failures, the average weight loss was 3·2 lb. a week over periods of 3 to 12 weeks.

Freed (1947) regarded ' Benzedrine ' as ' of inestimable value in controlling the desire for food and reducing the level of satiability to a more normal one '. His usual dose was one tablet t.i.d. half an hour to an hour before meals ; occasionally 2 tablets were required. A conclusive study by Harris et al. (1947) shows that the appetite-reducing effect of ' Benzedrine ' is such that obese patients can lose weight when allowed to eat all they want three or four times a day.

ERSNER, J. S. (1940). *Endocrinology*, **27**, 776.

FREED, S. C. (1947). *J. Amer. med. Ass.*, **133**, 369.

HARRIS, S. C., IVY, A. C., SEARLE, L. M. (1947). *J. Amer. med. Ass.*, **134**, 1468.

Functional Dysmenorrhœa

Of the half-dozen antispasmodic drugs which he has employed, Janney (1945) recommends ' Benzedrine ' Tablets as the most satisfactory in the symptomatic treatment of functional dysmenorrhœa, since they stimulate the patient's general mental outlook and relieve the characteristic cramps by relaxing uterine muscle spasm. According to Taylor (1941), ' Benzedrine ' relieved pain, fatigue, and depression in cases in which other measures had failed, giving complete relief in 40% and moderate relief in an equal number. In a series of 186 attacks of functional dysmenorrhœa reported in 91 working girls, 114 (61%) were completely relieved by the initial dose of 10 mg. ; 27 (15%) required a second dose, while in 45 (24%) medication seemed ineffective (Hundley et al., 1939).

Dosage.—Good results are obtained with a dose of 2 tablets given at the onset of the attack and repeated, if necessary, in four hours. In apprehensive women it is advisable to give 2 tablets on the morning of the two preceding days and on the morning of the first day of the period.

HUNDLEY, J. M. et al. (1939). *Med. Clin. N. Amer.*, **23**, 273 (March).

JANNEY, J. C. (1945). *Medical Gynecology*, Saunders, pp. 70, 302.

TAYLOR, Z. E. (1941). *New Engl. J. Med.*, **224**, 197.

Other Conditions

There are a number of published reports on the value of 'Benzedrine' when given with the anticonvulsant drugs in *epilepsy* and of its effectiveness in *sea-sickness*. It is sometimes helpful in *migraine*, *postural hypotension*, and numerous other complaints. It effectively dispels the *drowsiness* which may occur during treatment with antihistamine drugs such as 'Benadryl' and 'Pyribenzamine', but it in no way interferes with therapeutic response to these valuable preparations.

General Notes on Administration

Test Dose.—Occasional patients are hypersensitive to 'Benzedrine'; an initial test dose of one tablet is therefore recommended before embarking on a full course of treatment. This dose should be increased progressively until the optimum effect is reached. Administration in the late afternoon may interfere with sleep.

Contra-indications.—'Benzedrine' is contra-indicated wherever there is great excitability, marked anxiety, manic tendencies, or insomnia. Since the drug in large doses may have a pressor effect, it should be used with caution in hypertensive cases. Coronary disease and other serious heart conditions are definite contra-indications. 'Benzedrine' should be discontinued in patients who show by reactions to initial small doses that they are hypersensitive to it.

Side-effects.—Insomnia, irritability, restlessness, tension, anxiety, nausea, dryness of the mouth, and disturbance of the bowel habit may sometimes follow the use of 'Benzedrine' Tablets. These manifestations are infrequent when the therapeutic doses are employed, and they disappear on discontinuance of the drug or reduction of the dose. More serious reactions have occasionally been reported, but examination of these has generally shown them to be due to idiosyncrasy or want of care in administration.

Each 'Benzedrine' Tablet contains 5 mg. amphetamine sulphate

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For Smith Kline & French International Co.